

**Instructions:** Complete this template to provide IRB members and designated reviewers with sufficient information to conduct a substantive review of human research. If applicable, submit a Sponsor's Protocol in addition to this document. Detailed instructions for preparing this template can be found in the [Investigator's Manual](#). If the proposed human research is eligible for an Exemption Determination, see Appendix F of the [Investigator Manual](#).

GENERAL INFORMATION
<b>Protocol/ESTR Record Number (if assigned):</b>
<b>Version Number/Date: 30 January 2018</b>
<b>Principal Investigators: Dr. Katherine Semrau</b>
<b>Protocol Title: Verbal Autopsy of Maternal Deaths, Stillbirths, and Neonatal Deaths in BetterBirth</b>

## 1. Specific Aims

To conduct Verbal Autopsies of stillbirths and neonatal deaths identified in the BetterBirth trial to identify their potential causes, timing, and social determinants.

## 2. Background and Significance

### 2.1 Provide the scientific background and rationale for the research.

The BetterBirth trial was conducted to study the impact of the Safe Childbirth Checklist-based approach on maternal morbidity, maternal mortality, stillbirths and neonatal mortality for facility based deliveries in low resource settings. The trial was implemented in 120 health facilities (60 intervention and 60 control) spread across 24 districts in Uttar Pradesh.

The data collection for the BetterBirth trial completed in January 2017 and currently data analysis is in progress. On 2 March 2017, the preliminary findings were presented to Scientific Advisory Committee (SAC) appointed for the study. There were a total of 150 early maternal deaths, 7,455 stillbirths and early neonatal deaths out of the 157,689 mother-infant pairs that participated in the trial. It was observed that there was wide geographic variability in mortality across the study area. The Scientific Advisory Committee noted that it was essential to understand the causes, timing and social determinants of these deaths to better interpret the study results. Hence, the committee recommended undertaking verbal autopsies of deaths tracked in the study. Further, this exercise is also aimed to address potential misclassification of deaths (stillbirths and early neonatal deaths).

### 2.2 Describe the significance of the research, and how it will contribute to generalizable knowledge.

The verbal autopsy findings will be helpful to understand the result of the BetterBirth Trial. In addition, the findings will inform future investigations of maternal and newborn harm, especially those further upstream in health system and policy design.

### **3. Research Sites and Study Team**

#### **3.1. Identify and describe the sites or locations where the research will be conducted or overseen by the Harvard PI.**

The BetterBirth Trial was a facility-based study. However, the verbal autopsies of deaths identified during its course will be conducted at the current residence of the study participants.

#### **3.2. Is this a multi-site study?**

☐ No ☒ Yes: If yes, describe plans for communication among sites regarding adverse events, interim results, protocol modifications, monitoring of data, etc.

This study involves four Principal Investigators from two institutions: Drs. Vishwajeet Kumar and Aarti Kumar at Community Empowerment Lab (CEL) in Lucknow, Uttar Pradesh, India and Drs. Atul Gawande and Katherine Semrau at the Harvard TH Chan School of Public Health in Boston, MA, USA. The primary roles of the investigators are outlined below.

- Investigators from CEL (Drs. V. and A. Kumar) will oversee the research in the field and ensure the research is conducted in accordance with the protocol.
- Investigators from the Harvard Chan School (Drs. Gawande and Semrau) will provide key technical guidance to CEL and PSI–India.
  - Note: Population Services International (PSI) India, the primary implementation partner of the parent study, will be utilized as needed for recruitment purposes, as described in Section 18.4.

All investigators will be responsible for overall supervision of the research activities carried out by CEL in coordination with PSI–India. To this end, investigators will be in regular contact with each other and with project management and field staff.

#### **3.3. Is the research conducted outside the United States?**

☐ No ☒ Yes: If yes, describe local laws, regulations, and/or customs affecting the research.

There will be no significant differences between the regulation of this study in the United States and India.

#### **3.4. Are there any approvals or permissions that must be obtained from cooperating institutions, community leaders, government officials, including approval from another IRB or local research ethics committee?**

☐ No ☒ Yes: If yes, list the approvals/permissions and upload copies to the “Supporting Documents” page in ESTR.

Ethics approval for verbal autopsy has been submitted to the Institutional Review Boards at:

- Community Empowerment Lab, Lucknow, Uttar Pradesh, India
- Harvard School of Public Health, Boston, Massachusetts, United States
- Population Services International, Washington, DC, United States\*

\*With request to cede review to CEL.

The protocol will be registered with [clinicaltrials.gov](https://clinicaltrials.gov).

The parent study, “BetterBirth: Trial of the WHO Safe Childbirth Checklist Program” (Protocol #21975, ClinicalTrials.gov Identifier NCT02148952), received ethics approval with annual reviews from five Institutional Review Boards and the Indian Council for Medical Research (ICMR). Our local partner confirmed that ICMR approval is not required for this study.

**3.5. Describe the Principal Investigator’s experience conducting research at the study site(s) and familiarity with the local research context.**

Drs. Gawande and Semrau began working in Uttar Pradesh as co-Principal Investigators of BetterBirth: Trial of the WHO Safe Childbirth Checklist Program. Dr. V. Kumar and Ms. A. Kumar are native to India and currently reside in Uttar Pradesh. They co-founded Community Empowerment Lab (CEL), a scientific research and innovation organization based in Lucknow, Uttar Pradesh, India in 2011. CEL has expertise in conducting qualitative assessments (including verbal autopsies) in health care settings in Uttar Pradesh. Dr. V Kumar and Ms. A Kumar have been working in these communities and conducting research for over a decade. They have lead large studies which included conducting maternal and neonatal verbal autopsies. Dr. V. Kumar was a co-Principal Investigator of BetterBirth: Trial of the WHO Safe Childbirth Checklist Program.

**3.6. Describe how the Principal Investigator will ensure that sufficient time is devoted to conducting and completing the research.**

A detailed study timeline has been developed. Principal Investigators will ensure adherence to this timeline by closely coordinating with program managers and research staff.

**3.7. Describe how all research staff members are trained to ensure that they are adequately informed about the protocol and study-related duties.**

Data collectors will be trained by verbal autopsy experts at CEL on the standardized study tools and processes described in Section 4.6.

**3.8. Describe the minimum qualifications for each research role (e.g., RN, social worker, phlebotomist, statistician), their experience in conducting research, and their knowledge of the local research context.**

All data collectors will have a university-level degree (i.e., Bachelor's degree) in a research-related field such as social sciences. Coding of verbal autopsies will be completed by physicians holding MBBS and/or MD degrees. Data collectors and coders will be fluent in Hindi.

#### **4. Study Design**

##### **4.1. Describe the study design type.**

Verbal autopsy is a technique used to determine the cause of death by asking caregivers, friends or family members about signs and symptoms exhibited by the deceased in the period before death. This is usually done using a standardized questionnaire that collects details on signs, symptoms, complaints and any medical history or events. The cause of death, or the sequence of causes that led to death, are assigned based on the data collected by this questionnaire and on any other available information. The social autopsy tool is used in conjunction with the verbal autopsy tool to explore the non-biological factors contributing to a death, including the social, behavioural and health systems determinants of maternal and child deaths. This additional line of questioning has been identified as an important step to understand modifiable factors present in the home, community and health system, which can inform policies and practices for increasing access to and use of preventive and curative services. Rules and guidelines, algorithms or computer programmes, may assist in evaluating the information.

##### **4.2. Does the study involve more than one participant group?**

☐ No ☒ Yes: If yes, identify each group here and throughout all applicable sections.

Respondents for the neonatal deaths and stillbirths include mother or the family members of the baby. Mothers had consented to follow-up as part of the BetterBirth Trial.

##### **4.3. Indicate the duration of a participant's involvement.**

Participant involvement will be approximately 60 to 120 minutes. Participants may end the interview at any time and may request that the interview be completed in multiple sessions. Additional visits may be needed for data verification.

##### **4.4. Indicate the total number of participants to be screened (if applicable) and/or enrolled (i.e., signed consent form). If the proposed research involves secondary data analyses only, indicate the number of data, documents, records, and/or specimens that will be obtained.**

The mothers and/or family member(s) and community members of a subset of our perinatal mortality cases (170 cases) will be asked to participate.

#### **4.5. List inclusion and exclusion criteria, and describe the screening process.**

In order to be included in this study, one must be the mother or family member of an individual who was enrolled in the BetterBirth Trial and died. Women who did not consent to follow-up in the BetterBirth study will be excluded.

#### **4.6. Describe study procedures.**

The study will be conducted primarily by the study team at CEL with guidance and oversight provided by the study team HSPH. HSPH will be involved in tool design and revision, coding of social autopsies, and analysis plan development and execution.

The study team at CEL will adhere to the following study procedures for data collection, monitoring, and coding.

##### Data collection

Data will be collected using the WHO standard tools for conducting maternal, stillbirth or neonatal verbal autopsies, modified for the local context. A section on social autopsy will also be incorporated in the existing study instrument. These tools are standardized and adapted to use in these settings and have been implemented before in other studies in similar communities in U.P. (example: “AMANHI” and “Impact of topical application of cold-pressed sunflower seed oil with improved massage practices on neonatal mortality: a cluster randomized controlled trial in rural North India”). A team of specially trained data collectors (given the sensitive nature of the verbal autopsy questionnaire) will collect the data on existing Android based data collection platform.

Data will be collected by specially trained data collectors. They will collect the data at participants’ homes. Participants will include the mother (in case of neonatal death) and any additional person who was present during the events that led to the death. Additional interviewees may include the delivered mother’s husband, mother, mother-in-law, other family member, neighbor, etc. The delivered mother will be asked which individuals, if any, should be included in the interview. The mother and the individuals they indicate will be consented individually but interviewed together.

Each interview will take approximately 60 minutes.

The following data collection tools will be used together for interviews regarding neonatal deaths:

- Verbal Autopsy-Neonatal Death (NND) Tool
- Social Autopsy Tool
- Socioeconomic Status Tool

##### Data quality and safety



A team of specially trained data collectors will be hired. Data will be collected on tablets using a data collection platform that has in-built checks of missing values, range checks, skip patterns etc. to minimize the error in data collection. A GPS monitoring of location of interview will be conducted. The data will be checked at an aggregate level for heaping, interviewer-specific patterns, etc. Forms identified with errors will be sent back for verification and re-entry, but audit-trail will be captured to ensure that the full trail from original data and changes will be maintained with timestamp, GPS and user information. On-site quality assurance would involve both real-time data checks as well as GPS verification of the location of data collection. Data access will be restricted by users, with different privileges for data collectors, supervisors and study investigators. All personal identification information including names, etc. will be encrypted, and only a unique identification number to identify individuals will be made available for analysis. Data will be hosted over a secured network.

#### Physician coding

Every case will be coded for assigning underlying cause of death, antecedent causes and timing of death by trained and certified physicians. A WHO standard software and coding protocol will be used by these physicians to assign causes of death. The data collected through tablets will be sent to the central server. The narratives of every case will be collected on paper and a scan of the narrative will be sent along with the data. This entire data will be uploaded on the physician coding software from which the verbal autopsy cases will be allotted to physicians for coding. Each case will be independently coded by two physicians and in case of mismatch in the underlying cause of death between the two physicians, a third physician will independently code for the cause of death. Finally, if none of the three underlying causes of death match, a higher level physician arbitrator will resolve the case – this will be done to minimize unclassified deaths. A physician coordinator, who has extensive prior experience of coding verbal autopsy data will oversee the entire process and resolve issues with the help of supervisors of the data collection team. All the cases will be de-identified before uploading on the software for coding.

**4.7. Does the study involve the use of existing data, documents, records, and/or specimens for secondary analysis?**

☐ No ☒ Yes: If yes, indicate how, when, where, and from whom data, documents, records, and/or specimens will be obtained.

This study involves the use of existing data from the BetterBirth Trial (Protocol # 21975). Specifically, we will use mortality data collected as part of the BetterBirth Trial to identify cases of stillbirth/neonatal death. We will extract the names and contact information of patients who consented to be contacted for follow-up in order to re-contact patients to ask if they agree to participate in the verbal autopsy.

**4.8. Are there provisions for medical and/or psychological support resources available to participants (e.g., in the event of incidental findings, research-related stress)?**

☒ No ☐ Yes: If yes, describe the provisions and their availability.

**4.9. Is there a data and safety monitoring plan (required for greater than minimal risk studies)?**

☒ **No** ☐ **Yes: If yes, describe this plan.**

**4.10. Are there any anticipated circumstances under which participants will be withdrawn from the research without their consent?**

☒ **No** ☐ **Yes: If yes, describe the circumstances for withdrawal as well any associated procedures to ensure orderly termination, appropriate referrals, and/or follow-up care.**

## **5. Recruitment Methods**

**5.1. Does the study involve the recruitment of participants?**

☐ **No: If no, skip to the next section.**

☒ **Yes: If yes, indicate how, when, where, and by whom participants will be recruited.**

Participants will be recruited based on the inclusion criteria described in Section 4.5. Study staff members will first attempt to make contact with Accredited Social Health Activists (ASHAs), who are appointed by the National Rural Health Mission and act as conduits between patients and the health system. The data collector will attempt to call the relevant ASHA worker and request her assistance in establishing contact with the mother. The ASHA will be asked to provide a telephone number at which the mother can be reached, if possible. After this, the family will be initially contacted by study staff members via telephone. Individuals will be asked to participate in verbal autopsy, and, if they agree, a date and time for the interview will be determined. A data collector from CEL or PSI will visit the participant's home on an agreed-upon date and written consent will be obtained.

Final attempts at contact will be made via home visit if participants cannot be reached either via telephone or with ASHA engagement. Individuals who are reached at home will be introduced to the study and asked to participate using the appropriate recruitment script. For those individuals who agree to participate, data collectors will schedule a time to return to participants' homes for interviews to be conducted. (Note: Home visits are a culturally acceptable practice in this context; for example, home visits were used in the BetterBirth Trial for collection of 7-day outcomes of mothers and newborns.)

**5.2. Are there any materials that will be used to recruit participants, e.g., emails, posters, and/or scripts?**

☐ **No** ☒ **Yes: If yes, provide a list of the materials and upload copies to the "Consent Forms and Recruitment Materials" page in ESTR.**

Scripts will be used to recruit participants (see Stillbirth/Neonatal Death Recruitment Script).

## **6. Consent Process**

### **6.1. Will participants be invited to take part in the research?**

☐ **No: If no, explain why not.**

☒ **Yes: If yes, describe the consent process and upload consent materials to the “Consent Forms and Recruitment Materials” page in ESTR.**

A written informed consent will be administered to every participant prior to collection of data and standard consenting procedure followed. Consent will be obtained by the data collector at the participant’s home at the start of the scheduled visit. Data collectors will discuss all topics included in the consent form with the participant and answer any questions that the participant may have. All parties participating in an interview will be required to sign their own forms (except in cases involving illiterate participants\*). Husbands, mothers, mothers-in-law, etc. of the delivered woman cannot consent on her behalf; she is free to consult her family in her decision to participate but ultimately must consent herself.

\*In cases involving illiterate participants, the name and signature/thumbprint of a literate witness will be obtained, as is required by the local IRB.

### **6.2. Will the consent process involve obtaining signature?**

☒ **Yes** ☐ **No: If no, explain why not.**

### **6.3. Will signature be documented by another method, e.g., thumbprint?**

☐ **No** ☒ **Yes: If yes, describe this method and explain how this is appropriate given the local research context, population, etc.**

If a participant is unable to provide a written signature, a thumbprint will be used to document consent. In order to facilitate this documentation, the data collector will be equipped with an inepad when deploying to the field. The use of a thumbprint is culturally appropriate and equivalent to a signature in this setting; the local IRB requires that we offer this method of documentation.

### **6.4. Will participants be offered a copy of the consent information?**

☒ **Yes** ☐ **No: If no, explain why not.**

### **6.5. Will consent information be provided in a language other than English?**

☐ **No** ☒ **Yes: If yes, identify the language(s) that consent information will be provided, identify who will be responsible for translation, and the provisions for communicating this information to participants.**

The consent form will be primarily available in Hindi. This Hindi consent form has been used in previous studies and has been verified by study partners.

## **7. HIPAA Privacy Protections**

### **7.1. Does this research involve the collection or use of protected health information (PHI) from a hospital, health center, health plan, or health insurance plan, or the Harvard Dental Center?**



☐ **No: If no, skip to the next section.**

☒ **Yes: If yes, describe plans for obtaining authorization to access protected health information or provide the rationale for a waiver of authorization.**

This study will utilize PHI from its parent study, the BetterBirth Trial. Drs. V. Kumar, Gawande, and Semrau are Principal Investigators on both studies. Therefore, data from the BetterBirth Trial will be used at the discretion of the investigators towards completing the specific aims of the verbal autopsy work. For example, BetterBirth Trial data (i.e., PHI of deceased mothers/infants) will be used to identify, contact, and recruit potential participants. PHI may include mother's name, husband's name, contact number(s), address, date of delivery, and other fields needed to confirm participant's identity at the time of recruitment.

## **8. Vulnerable Populations**

**8.1. Does the research involve vulnerable populations (e.g., children; pregnant women, human fetuses, neonates; prisoners; elderly; economically disadvantaged; employees or students of the investigator or sponsor; undocumented individuals; refugees; illiterate or low-literacy; military personnel; terminally ill; cognitively impaired or mentally ill; persons with a stigmatizing disease or condition, e.g. AIDS/HIV, etc.)?**

☐ **No: If no, skip to the next section.**

☒ **Yes: If yes, identify all vulnerable populations and describe safeguards to protect their rights and welfare.**

Vulnerable populations include:

- Low-literacy or illiterate individuals
  - To protect the rights and welfare of low-literacy or illiterate individuals, the name and signature/thumbprint of a literate witness will be required for consent.
- Bereaved individuals
  - To protect the rights and welfare of bereaved individuals, participation in the verbal autopsy will be voluntary and can be refused or withdrawn at any time.

## **9. Risks (Risks may include physical, psychological, social, legal, reputational, and/or financial)**

**9.1. Describe the reasonably foreseeable risks, discomforts, and/or inconveniences to participants and/or the group/community to which they may belong. Indicate the probability, magnitude, and duration of each risk.**

It may be psychologically or emotionally taxing for mothers or family member(s) to be interviewed about the deceased and details about the death. Interviews will take place well after the culturally appropriate mourning period of 14-40 days has passed. Interviewers will be trained in techniques for the handling of sensitive interviews.

**9.2. Identify whether any of the information collected, if disclosed outside of the research, could reasonably place the participant at risk of criminal or civil liability or be damaging to the participant's financial standing, employability, insurability, or reputation.**

It is possible that a verbal autopsy may indicate that an unnatural cause (accidental or intentional) contributed to a death. [1] Deaths may have occurred at the hospital at the time of childbirth or outside of the hospital up to seven days after childbirth. Disclosure of an unnatural death could place participant(s) at risk of criminal or civil liability or be damaging to the participant's financial standing, employability or reputation. Note: In CEL's experience of conducting a large number of verbal autopsies for previous studies, no such situation has been encountered.

**9.3. Outline provisions in place to minimize each risk identified above.**

To minimize this risk of psychological or emotional distress, data collectors will be trained in conducting sensitive interviews. To minimize the risks associated with unnatural death, neither the Principal Investigators nor other study team members will report suspicious deaths to local authorities or IRBs. (Note: There are no mandatory reporting requirements in India.) Nondisclosure will reduce the risks to participants stated above as well as the risk of retribution against the reporter. Additionally, all names and identifying information of the deceased and the respondent(s) will be removed (i.e., de-identified) prior to uploading to the software for coding. The final dataset and transcript will be de-identified and reporting will be done at the aggregate level.

**10. Benefits**

**10.1. Describe the potential benefits to participants and society.**

Verbal autopsies may shed light on important public health factors related to deaths in the community. This will not offer a direct benefit to the families, it benefits society in that we will understand more about causes of death in this population. It will also help in the design of new interventions to prevent these deaths.

**11. Participant Privacy**

**11.1. Describe provisions to protect participants' privacy (their ability to control and limit the extent, timing, and circumstances of sharing information about themselves with others, e.g., the use of a private interview room) and to minimize any sense of intrusiveness that may be caused by study questions or procedures.**

Voluntary Participation

Participation in the verbal autopsy will be entirely voluntary. It is one's choice whether to participate or not. Individuals will not be penalized in any way should they choose not to participate. Individuals may stop participating at any time.

Confidentiality

All the information that will be collected as a part of the verbal autopsy will be strictly confidential. Data will be coded using indirect identifiers. Interviewees' identifiable information will be available only to key members of the research teams at CEL and HSPH. Deceased individuals' information is coded using indirect identifiers in the BetterBirth dataset.

Right to Refuse or Withdraw

Participants do not have to take part in this verbal autopsy if they do not wish to do so. They may stop participating in the verbal autopsy at any time they choose. It is their choice and all their rights will be respected.

## **12. Data Confidentiality**

### **12.1. Indicate the identifiability of the data/specimens:**

- ☐ Data/specimens will not contain any direct or indirect identifiers (anonymous data).
- ☐ Data/specimens will contain direct or indirect identifiers, but the research team will remove them upon receipt (de-identified data).
- ☒ Data/specimens will contain indirect identifiers (i.e., number, letter, symbol, or combination thereof) and the research team will maintain a key that links identifiers to individual participants (coded data).
- ☐ Data/specimens will contain direct identifiers (identifiable data).
- ☐ None of the above; describe:

### **12.2. Identify where data will be stored, e.g., on campus at Harvard or remotely, and describe the provisions to maintain confidentiality (e.g., password protection, encryption, locked filing cabinets, etc.). Refer to the [Investigator Manual](#) and the [Harvard Research Data Security Policy](#) for additional information.**

Verbal autopsy data will be hosted by CEL on encrypted server secured under multiple layers of cyber security. The data will be shared with HSPH, where it will also be kept on an encrypted server. Signed consent forms will be kept in locked filing cabinets in a secure facility maintained by CEL in Uttar Pradesh, India.

### **12.3. Describe whether any data will be transmitted and, if so, how, when, and to whom.**

Data needed to identify, contact, and recruit study participants will be transmitted from HSPH to CEL (and potentially PSI, pending their role in the execution of this work) at the initiation of research activities via a secure data transfer. Data resulting from the verbal autopsies will be transmitted from CEL to HSPH at various intervals as the data are collected via a secure data transfer. Additionally, the verbal autopsy narratives will be securely transferred between HSPH and translation agencies for the purpose of translation from Hindi into English. HSPH and the translation agency will jointly sign a Data Use/ Non-Disclosure Agreement to outline protections for the data and appropriate handling procedures. All HSPH staff handling the data are CITI trained and will ensure the translation agency clearly understands the requirements about data storage and transfer (as outlined in the DUA/NDA).

**12.4. Indicate who is responsible for data management and how the research team and/or other collaborators are permitted access to information.**

Technical personnel at CEL and HSPH are responsible for data management. Data exports from the database will be made accessible to Principal Investigators and key members of the CEL and HSPH teams.

**12.5. Indicate how long data will be stored and describe the plans for data at the end of the storage period (e.g., is data destroyed, returned to data provider, etc.).**

The data will be stored on secure servers at HSPH (Level 4 Compliant) and CEL. As per a local requirement set by the Indian Council of Medical Research, the storage period is indefinite. It will be maintained for at least seven years in accordance with the Harvard requirement. Hard copies of consent forms will also be kept for seven years in locked file cabinets at a storage facility maintained by CEL in Uttar Pradesh.

**13. Data/Statistical Analyses Plan**

**13.1. Describe plans for analysis (including the statistical method, if applicable).**

The physician coded causes of death will be used to understand the cause structure of newborn deaths and stillbirths for institutional births. The biomedical cause of deaths will be assessed in light of the social determinants as captured in the social autopsy component of the questionnaire to further identify gaps in service delivery and potential points of intervention.

**13.2. Is there a sample size/power calculation?**

☒ No ☐ Yes: If yes, describe the calculation and the scientific rationale, and, if applicable, by site and key characteristics such as participant demographics.

**14. Costs and Compensation**

**14.1. Identify any costs that participants may incur during the study, including transportation costs, childcare, or other out-of-pocket expenses.**

Participants will not incur any costs during the study.

**14.2. Identify remuneration that participants may receive during the study. Specify the amount, timing of disbursement, and method (e.g. money, gift cards, in-kind, incentives, raffles, and transportation). Describe how compensation will be calculated and paid if a participant withdraws. If any participant will receive a single payment more than \$100, or \$600 or more in one calendar year, Social Security Number must be collected. Refer to [Harvard University Financial Policy on Human Subject Payments](#).**

Participants will not receive any remuneration.



## **15. Sharing Study Results**

### **15.1. Is there a plan to share study results with individual participants and/or the participant group/community?**

☐ No ☒ Yes: If yes, describe the plan.

As per local IRB requirements, data sharing meetings will be held with the facility, district and state officials that participated in the BetterBirth Trial to inform relevant stakeholders of the verbal autopsy findings (i.e., causes of death in the community). After these meetings, we will publish the results so that other interested people may learn from the research. At the end of this study, de-identified data from verbal autopsy will be shared in a public domain.

## **16. Device**

### **16.1. Does the research involve a Device?**

☒ No: If no, skip to the next section.

☐ Yes: If yes, describe the device, including the generic or common name, brand name (if applicable), purpose, function/operation, and whether it is an implant. Indicate who is providing this device for research use.

### **16.2. Indicate the FDA status of the device as it is being used for the proposed research:**

☐ FDA-approved device being used “on-label” (i.e., FDA-approved purpose, population, manner).

☐ FDA-approved device that is being used “off-label” (i.e., for a different purpose, population, or in a different manner than approved).

☐ Not approved by the FDA.

### **16.3. Indicate the IDE Status of this device:**

☐ The use of this device has an IDE.

☐ The use of the device qualifies for an Abbreviated IDE.

☐ Not use of the device is exempt from the IDE requirements.

### **16.4. Has the FDA made a determination as to whether the device is Significant Risk or Non-Significant Risk? ☐ No ☐ Yes: If yes, indicate the FDA’s determination.**

### **16.5. Describe plans for storage control, and dispensing of the product so that (1) only authorized investigators will use the product; (2) the product will only be used in participants who have provided consent, and (3) there will be documented tracking of each product, including unique identifiers and any return/disposal.**

## **17. Drug/Biologic**

### **17.1. Does the research involve a Drug or Biologic?**

☒ No: If no, skip to the next section.



☐ **Yes:** If yes, describe the drug or biologic, including the generic or common name, brand name (if applicable), dosing, route of administration, number of doses, timing of administration. Indicate who is providing the drug, biologic, supplement for research use.

**17.2. Indicate the IND Status of this drug or biologic:**

- ☐ There is an IND approval from the FDA for the use of this item.  
☐ An IND application has been, or will be, submitted to the FDA.  
☐ An IND approval is not required.

**17.3. Describe how dispensing, delivery and administration will be performed, and by whom. Include information about control (e.g., locked storage), tracking (e.g., lot number, returned pills), documentation, and return/disposal.**

**18. Data or Specimen Banking (Repositories)**

**18.1. Does the study include establishing a repository for sharing data or specimens?**

- ☐ **No:** If no, skip to the next section  
☒ **Yes:** If yes, identify what data or specimens will be collected for the repository and what information will be associated with the data or specimens

A de-identified data repository will hold the verbal autopsy data collected. Please see the verbal autopsy tool for data fields. At the end of the study, de-identified data will be shared in a public domain.

**18.2. Describe where and how long the data/specimens will be stored and whether participants' permission will be obtained to use the data/specimens in other future research projects.**

In accordance with Indian regulations, the data will be available both at HSPH and with the local PI. During the consent process, participant permission will be obtained to include their de-identified data from the verbal autopsy in a public domain.

**18.3. Identify who may request access to the data/specimens and describe this process.**

The Gates Open Access Policy requires unrestricted access of all peer-reviewed published research funded by the foundation, including underlying datasets. All requests for data will be routed through HSPH study team. Co-Principal Investigators from CEL will receive IRB approval from the local IRB.

**18.4. Will data/specimens be sent to research collaborators outside of Harvard?**

- ☐ **No** ☒ **Yes:** If yes, describe the plan and upload any agreements to the "Supporting Documents" page in ESTR.

Information needed to identify the mother and/or family member(s) of deceased individuals (such as case ID, patient ID, family name, address, phone number, facility

number, date of admission, date of delivery, and ASHA contact) from the parent study will be shared by HSPH to the study partner(s) (CEL and PSI, pending PSI's role in the execution of this work). We have a Data Use Agreement outlining this data transfer.

**18.5. Will data/specimens be received from collaborators outside of Harvard?**

☐ No ☒ Yes: If yes; describe the plan and upload any agreements to the "Supporting Documents" page in ESTR.

Verbal autopsy data collected by CEL will be shared with HSPH. We will develop a Data Use Agreement specifying the plan.

**19. Research Related Injuries** (required for research posing greater than minimal risk)

**18.1 Are there provisions for medical care and compensation for research-related injuries?**

☒ No ☐ Yes: If yes, outline these provisions. Although Harvard's policy is not to provide compensation for physical injuries that result from study participation, medical treatment should be available including first aid, emergency treatment and follow-up care as needed. If the research plan deviates from this policy, provide appropriate justification.

**20. Reportable Events**

**20.1. Outline plans for communicating reportable events to the IRB, Sponsor, or others as applicable (e.g., adverse events, unanticipated problems involving risks to participants or others, breach of confidentiality).**

Any reportable new information will be brought to the attention of the IRB in necessary instances as determined by the Principal Investigators in India and at HSPH within 5 days.

**21. Regulatory Compliance**

**21.1. Describe plans for monitoring regulatory compliance, in order to ensure proper record keeping, retention of required regulatory documents, and adherence to the IRB-approved protocol and/or IRB policies and procedures.**

The co-Principal Investigators at CEL will be primarily responsible for monitoring regulatory compliance at the local level. The local co-PIs will oversee the day-to-day data collection activities, including monitoring the data collection and storage to ensure processes follow the protocol. They have confirmed that this protocol is in alignment with local regulations and will alert co-PIs at HSPH should regulations change. Additionally, the HSPH team will hold frequent check-ins with the co-PIs and data collection team in India to confirm that activities are moving forward in line with ethical guidelines. The HSPH team will report updates to our regulatory documents to our IRBs on a regular basis as required.

**22. Clinical Trials**

**22.1. Is this an NIH funded clinical trial or an applicable trial (ACT) under the [FDA Amendments Act](#)?**

☒ **No** ☐ **Yes:** If yes, describe your plan for registering this project in a clinical trials registry, e.g., [clinicaltrials.gov](https://clinicaltrials.gov). Provide the registry record number, if available.